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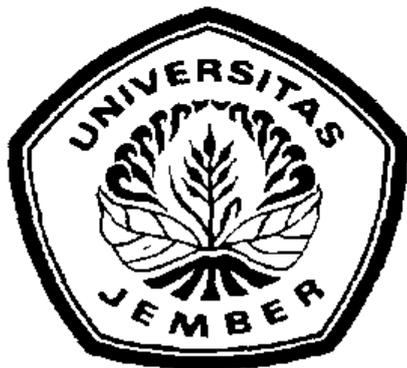
**DIFFERENCES IN THE EFFECTIVENESS OF SELECTIVE ALPHA
BLOCKER THERAPY COMBINED WITH 5-ALPHA REDUCTASE
INHIBITOR ON IPSS VALUE OF BPH LUTS PATIENTS**

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CHARACTERISTIC OF IATROGENIC BLADDER TRAUMA PATIENT IN HASAN SADIKIN GENERAL HOSPITAL FROM JANUARY 2013 - JANUARY 2018

Muhammad Ilhamul Karim, Kuncoro Adi



DIFFERENCES IN THE EFFECTIVENESS OF SELECTIVE ALPHA BLOCKER THERAPY COMBINED WITH 5-ALPHA REDUCTASE INHIBITOR ON IPSS VALUE OF BPH LUTS PATIENTS

Septa Surya Wahyudi, Nuno Febrina Probosutiksna, Enny Suswati



COMPARISON OF PAIN PERCEPTION BETWEEN INTRAVENA TRAMADOL INJECTION WITH PERIPROSTATIC LIDOCAINE INJECTION IN TRANSRECTAL ULTRASONOGRAPHY GUIDED PROSTATE BIOPSY PATIENT

Zuhri Sawal, Wahjoe Djatsoesanto, Tarmono Djojodimedjo



THE EFFECT OF VITAMIN E (α - TOCOPHEROL) AS NEPHROPROTECTOR ON BLOOD UREA NITROGEN AND SERUM CREATININE LEVEL OF STRAIN WISTAR RATS AFTER CISPLATIN TREATMENT: IN VIVO STUDY



DIFFERENCES IN THE EFFECTIVENESS OF SELECTIVE ALPHA BLOCKER THERAPY COMBINED WITH 5-ALPHA REDUCTASE INHIBITOR ON IPSS VALUE OF BPH LUTS PATIENTS

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ABSTRACT

Objective: The purpose of this study is to know the differences in effectiveness between SAB administration with combination 5-ARI administration assessed by IPSS evaluation in BPH LUTS patients. **Material & Methods:** This observational analytic with a cross-sectional design study had been done to 50 BPH LUTS patients that obtained at Paru Jember, Bina Sehat Jember, and Bhayangkara Bondowoso Hospital. These samples had got by simple random sampling method and include in inclusion with exclusion criteria freely. **Results:** This comparison study between the type of medical therapy administration and total IPSS decrease, IPSS-voiding decrease, IPSS-storage decrease, IPSS-QoL, and prostate volume give significancies as follows: $p=0.002$; $p<0.001$; $p<0.001$; $p<0.05$; $p<0.001$. **Conclusion:** There are significant differences between the type of medical therapy (SAB or 5-ARI combination) and total IPSS decrease, IPSS-voiding decrease, IPSS-storage decrease, IPSS-QoL, and prostate volume.

Keywords: Benign prostatic hyperplasia (BPH), Lower Urinary Tract Syndrome (LUTS), International Prostatic Symptom Score (IPSS), Selective Alpha Blocker, 5-Alpha Reductase Inhibitor.

ABSTRAK

Tujuan: Mengetahui adanya perbedaan efektivitas pemberian monoterapi Selective Alpha-Blocker dengan kombinasi 5-Alpha Reductase Inhibitor yang dinilai melalui penilaian IPSS pada pasien BPH LUTS. **Bahan & Cara:** Jenis penelitian adalah analitik observasional dengan desain cross-sectional yang telah dilakukan pada 50 pasien BPH LUTS di RS. Paru Jember, RS. Bina Sehat Jember, dan RS. Bhayangkara Bondowoso. Sampel-sampel ini didapat dengan metode sederhana random sampling dan dimasukkan dalam inklusi dengan kriteria eksklusi secara bebas. **Hasil:** Studi perbandingan antara jenis administrasi terapi medis dan penurunan IPSS total, penurunan IPSS-voiding, penurunan penyimpanan IPSS, IPSS-QoL, dan volume prostat memberikan signifikansi sebagai berikut: $p=0.002$; $p<0.001$; $p<0.001$; $p<0.05$; $p<0.001$. **Simpulan:** Terdapat perbedaan yang signifikan antara jenis terapi medis (kombinasi SAB atau 5-ARI) dan total IPSS decerese, penurunan voiding IPSS, penurunan penyimpanan IPSS, IPSS-QoL, dan volume prostat.

Kata Kunci: Benign Prostatic Hyperplasia (BPH), Lower Urinary Tract Syndrome (LUTS), International Prostatic Symptom Score (IPSS), Selective Alpha Blocker, 5-Alpha Reductase Inhibitor.

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INTRODUCTION

Benign Prostatic Hyperplasia (BPH) can inhibit the process of urination and the impact on the quality of men's life. This process arises from the age of 30 years with an increased risk factor up to the age of 60 years.¹ BPH can provide some conditions, such as narrowing of the prostatic urethrae duct, increasing prostate volume, the appearance of the

Lower Urinary Tract Syndrome (LUTS), and urinary retention.² LUTS are several symptoms in the lower urinary tract which can be classified into three types, namely storage, voiding, and post-micturition. International Prostatic Symptom Score (IPSS) is one method of WHO measurement that can be used to assess LUTS in BPH patients. IPSS has several criteria, including the degree by a score of 0-7 as a light symptom, moderate with a score of 8-19, and

severity with a score of 20-35.³ A research by Amalia through case studies in dr. Kariadi, Sultan Agung, and Roesmani Semarang Hospitals have reported that men aged ≥ 50 years had a risk of 6.24 times (95% CI: 1.71 to 22.99) higher than in men aged <50 years.⁴

Medical treatment in patients with BPH LUTS aims to improve prostate smooth muscle resistance as a dynamic component and prostate volume growth as a static component. Some medication agents that can be given are Selective-Alpha Blocker (SAB), 5-Alpha Reductase Inhibitors (5-ARI), and Phosphodiesterase Type 5 Inhibitors.⁵ SAB works by relaxing prostate and bladder neck's muscle to reduce their resistance due to excessive contraction of that muscle and 5-ARI to inhibit the conversion process of testosterone into Dihydrotestosterone (DHT). The SAB provision as first-line monotherapy for BPH LUTS case provides symptomatic improvement which is calculated by IPSS value and an increase in urinary flow rate. SAB and 5-ARI combination as a first-line therapy gives better results than monotherapy administration like SAB or 5-ARI.⁵ There is no research data in which has been done regarding differences in the effectiveness of using SAB 5-ARI combination in Jember, Indonesia through comparative IPSS assessment in patients with BPH LUTS.

OBJECTIVE

Knowing the different effectiveness of monotherapy Selective Alpha-blocker (SAB) in combination with 5-Alpha Reductase Inhibitor (5-ARI) to the judgment of the International Prostatic Symptoms (IPSS) value in BPH patients with LUTS. The specific objectives of this study as follows:

- 1) Knowing the different effectiveness between SAB administration and 5-ARI combination to the decline in IPSS total score in BPH LUTS patients.
- 2) Knowing the different effectiveness between SAB administration and 5-ARI combination to the decline in IPSS-voiding score in BPH LUTS patients.
- 3) Knowing the different effectiveness between SAB administration and 5-ARI combination to the decline in IPSS-storage score in BPH LUTS patients.

MATERIAL & METHODS

This study used an observational analytic method with a cross-sectional design. This study had

been done to BPH LUTS patients from October 2018 to January 2019 at Paru Jember, Bina Sehat Jember, and Bhayangkara Bondowoso Hospital. This research used simple random sampling from 537 patients who received medical therapy, found 50 patients met the inclusion criteria and exclusion criteria freely. This study used primary data through guided interviews and secondary data through the medical records of patients. Secondary data were obtained in the form of demographic data, type of medical therapy, and ultrasonography results sample. Shapiro-Wilk test was used for distribution from research data. Bivariate parametric used independent t-tests and non-parametric by using the Mann-Whitney test.

Inclusion criteria for the sample are as follows: (1) Men with at least 50 years of age; (2) Patients with a clinical diagnosis of BPH with Lower Urinary Tract Syndrome (LUTS); (3) Patients with BPH LUTS medical monotherapy or combination for at least 3 months with Urologist recommendation; (4) BPH LUTS patients willing to be sampled in this research.

Exclusion criteria for the sample are as follows: (1) Patients with prostate cancer at first diagnosis or the first three months of medical treatment with evidence in the form of biopsy results for investigations by the Clinical Pathologist; (2) Patients with a history of diabetes mellitus, diabetes insipidus, and neurological disorders; (3) Patients with a history of prostate surgery treatment; (4) Patients with a history of bladder disorders such as bladder stones, bladder tumors, and cystitis; (5) Patients with a history of urethral tract disorders in the form of meatal stenosis, urethral stricture, urethral stones, urethral tumors, and urinary tract infections; (6) Have an incomplete medical record.

RESULTS

Table 1 illustrates the 25 sample recipients monotherapy in Bina Sehat Jember Hospital, Paru Hospital in Jember, and Bhayangkara Bondowoso Hospital, data showed a decrease in IPSS total as follows: 2 samples (8%) fell 8 points, 7 samples (28%) decreased 9 points, 7 samples (28%) experienced down 10 points, 6 samples (24%) fell 11 points, and 3 samples (12%) experienced a decrease in IPSS total of 12 points.

Table 2 illustrates the 25 sample recipients of combination therapy in the hospital. Bina Sehat Jember Hospital, Paru Hospital in Jember, and Bhayangkara Bondowoso Hospital, data showed a

Table 1. The total frequency of decreased IPSS in monotherapy sample groups.

No	Total IPSS reduction (points)	Total (n)	Percentage (%)
1	8	2	8%
2	9	7	28%
3	10	7	28%
4	11	6	24%
5	12	3	12%
	Total	25	100%

Table 2. Frequency decrease of total IPSS in combination therapy sample group.

No	Total IPSS reduction (points)	Total (n)	Percentage (%)
1	13	2	8%
2	14	3	12%
3	15	4	16%
4	16	2	8%
5	17	5	20%
6	18	4	16%
7	19	1	4%
8	20	4	16%
	Total	25	100%

Table 3. Frequency of impairment of IPSS-voiding on monotherapy sample groups.

No	Reduction of IPSS-Voiding (points)	Total (n)	Percentage (%)
1	4	2	8%
2	5	6	24%
3	6	9	36%
4	7	3	12%
5	8	3	12%
6	9	2	8%
	Total	25	100%

decrease in IPSS total as follows: 2 samples (8%) fell 13 points, 3 samples (12%) experienced a decline of 14 points, 4 samples (16%) experienced a decline of 15 points, 2 samples (8%) fell 16 points, 5 samples (20%) decreased 17 points, 4 samples (16%) fell 18 points, one sample (4%) declined 19 points, and 4 samples (16%) experienced a decrease in IPSS total of 20 points.

Table 3 describes the 25 recipient samples monotherapy in Bina Sehat Jember Hospital, Paru Hospital in Jember, and Bhayangkara Bondowoso

Hospital, data showed a decrease in IPSS-voiding as follows: 2 samples (8%) declined 4 points, 6 samples (24%) decreased 5 points, 9 samples (36%) decreased 6 points, 3 samples (12%) decreased 7 points, 3 samples (12%) fell 8 points, and 2 samples (8%) experienced a decrease in IPSS-voiding up to 9 points.

Table 4 illustrates the 25 sample recipients of combination therapy in the hospital. Bina Sehat Jember Hospital, Paru Hospital in Jember, and Bhayangkara Bondowoso Hospital, data showed a

decrease in IPSS-voiding as follows: 1 sample (4%) declined 5 points, 2 samples (8%) experienced a decline of 6 points, 3 samples (12%) decreased 7 points, 6 samples (24%) decreased 9 points, 6 samples (24%) fell 10 points, 2 samples (8%) fell 11 points, 2 samples (8%) fell 12 points, 2 samples (8%) fell 13 points, and 1 sample (4%) experienced a decrease in IPSS-voiding reach 14 points.

Table 5 illustrates 25 samples monotherapy recipients in Bina Sehat Jember Hospital, Paru Hospital in Jember, and Bhayangkara Bondowoso Hospital, data showed a decrease in IPSS-storage as

follows: 9 samples (36%) decreased 1 point, 6 samples (24%) dropped 2 points, 7 samples (28%) decreased 3 points, and 3 samples (12%) experienced a decrease in IPSS-storage 4 points.

Table 6 illustrates the 25 sample recipients of combination therapy in the hospital. Bina Sehat Jember Hospital, Paru Hospital in Jember, and Bhayangkara Bondowoso Hospital, data showed a decrease in IPSS-storage as follows: 4 samples (16%) dropped 2 points, 4 samples (16%) decreased 3 points, 8 samples (32%) decreased 4 points, 1 sample (4%) declined 5 points, 2 samples (8%)

Table 4. Frequency of impairment of IPSS-voiding on monotherapy sample groups.

No	Reduction of IPSS-Voiding (points)	Total (n)	Percentage (%)
1	5	1	4%
2	6	2	8%
3	7	3	12%
4	9	6	24%
5	10	6	24%
6	11	2	8%
7	12	2	8%
8	13	2	8%
9	14	1	4%
	Total	25	100%

Table 5. Frequency of decrease IPSS-storage in monotherapy sample groups.

No	Reduction of IPSS Storage (points)	Total (n)	Percentage (%)
1	1	9	36%
2	2	6	24%
3	3	7	28%
4	4	3	12%
	Total	25	100%

Table 6. Frequency Decrease IPSS-storage in combination therapy sample group.

No	Reduction of IPSS Storage (points)	Total (n)	Percentage (%)
1	0	1	4%
2	2	4	16%
3	3	4	16%
4	4	8	32%
5	5	1	4%
6	6	2	8%
7	8	2	8%
8	9	2	8%
9	11	1	4%
	Total	25	100%

experienced a decline of 6 points, 2 samples (8%) fell 8 points, 2 samples (8%) fell 9 points, and 1 sample (4%), which dropped 11 points IPSS-storage.

Table 7 describes the 25 recipient samples monotherapy in Bina Sehat Jember Hospital, Paru Hospital in Jember, and Bhayangkara Bondowoso Hospital, data showed a decrease in IPSS-QoL as follows: 9 samples (36%) decreased 1 point, 9 samples (36%) dropped 2 points, and 5 samples (20%) decreased up to 3 points.

Table 8 describes the 25 sample recipients of combination therapy in the hospital. Bina Sehat Jember Hospital, Paru Hospital in Jember, and Bhayangkara Bondowoso Hospital, data showed a

decrease in IPSS-QoL as follows: 4 samples (16%) decreased 1 point, 4 samples (16%) dropped 2 points, 6 samples (24%) decreased 3 points, 6 samples (24%) decreased 4 points and 2 samples (8%) decreased to 5 points.

Table 9 describes the 25 recipient samples monotherapy in Bina Sehat Jember Hospital, Paru Hospital in Jember, and Bhayangkara Bondowoso Hospital, data showed 10 samples (40%) had a prostate volume of 21-25 mL, 13 samples (52%) had a prostate volume of 25-30 mL, and 2 samples (8%) have a prostate volume of 31-35 mL.

Table 10 describes the 25 sample recipients of combination therapy in the hospital. Bina Sehat

Table 7. Frequency of decreasing IPSS-QoL in monotherapy sample groups.

No	Reduction of IPSS <i>QoL</i> (points)	Total (n)	Percentage (%)
1	0	2	8%
2	1	9	36%
3	2	9	36%
4	3	5	20%
	Total	25	100%

Table 8. Frequency Decrease IPSS-QoL in combination therapy sample group.

No	Reduction of IPSS <i>QoL</i> (points)	Total (n)	Percentage (%)
1	0	3	12%
2	1	4	16%
3	2	4	16%
4	3	6	24%
5	4	6	24%
6	5	2	8%
	Total	25	100%

Table 9. Frequency of prostate volume in monotherapy sample group.

No	Prostate Volume Classification	Total (n)	Percentage (%)
1	21-25 mL	10	40%
2	25-30 mL	13	52%
3	31-35 mL	2	8%
	Total	25	100%

Table 10. Frequency of prostate volume in combination therapy sample group.

No	Prostate Volume Classification	Total (n)	Percentage (%)
1	30-40 mL	8	32%
2	41-60 mL	8	32%
3	61-90 mL	9	36%
	Total	25	100%

Table 11. Results of the comparative test of T-Test between types of therapy on the decline of IPSS total.

Type of Therapy Given	Mean ± Std. Error Mean	P-Value	Interval (IK95%)
Monotherapy (alpha blocker)	10.04 ± 0.23438	0.002	6.6 (5.58–7.61)
Combination therapy (alpha blocker + 5-alpha reductase inhibitor)	16.64 ± 0.44302		

Table 12. Results of the Mann-Whitney comparative test between the types of therapy on prostate volume, the reduction of IPSS-voiding, IPSS-storage, and IPSS-QoL.

No	Variable	Type of Therapy Given
1	Prostate Volume	p<0.001
2	Reduction of IPSS <i>Voiding</i>	p<0.001
3	Reduction of IPSS <i>Storage</i>	p<0.001
4	Reduction of IPSS QoL	p<0.05

Jember Hospital, Paru Hospital in Jember, and Bhayangkara Bondowoso Hospital, data 8 samples (32%) had a prostate volume of 30-40 mL, 8 samples (32%) had a prostate volume of 41-60 mL, and 9 samples (36%) have a prostate volume of 61-90 mL.

Table 11 shows the 50 samples of patients with BPH LUTS in Bina Sehat Jember Hospital, Paru Hospital in Jember, and Bhayangkara Bondowoso Hospital. The test results of the T-test give $p=0.002$ which indicates the null hypothesis (H_0) is rejected and there is a significant difference between the type of treatment given to the reduction in total IPSS. In monotherapy administration, the total IPSS score decreased by an average score of 10.04 points and the standard error of 0.23 while the combination therapy provides a decrease in IPSS total score by the average value of 16.64 points and a standard deviation of 0.44.

Table 12 describes 50 patient samples BPH LUTS in Bina Sehat Jember Hospital, Paru Hospital in Jember, and Bhayangkara Bondowoso Hospital, non-parametric tests Mann-Whitney gives a p -value<0.05, which indicates the null hypothesis (H_0) is rejected and there is a significant difference between the type of therapy given to lowering the IPSS-voiding, IPSS-storage, IPSS QoL, and prostate volume.

DISCUSSION

Table 11 describes the significant difference between the type of treatment given to the reduction in total IPSS. Giving the 5-Alpha Reductase

Inhibitor can inhibit an increase in prostate volume as the main pathophysiology of BPH disease. The impact given in the form of risk reduction ball valve obstruction and overuse detrusor monotherapy activity through the provision of that total IPSS score provides a greater reduction than the administration of alpha-blocker monotherapy. In accordance with the results of the study, describe the combination therapy may provide an improvement of clinical symptoms and reduce the need for surgical treatment of BPH patients with LUTS.⁶ Furthermore, state combination therapy may provide a reduction in total IPSS ≥ 4 points compared to administration of monotherapy in patients with BPH LUTS.⁷

Tables 3 and 4 illustrate the significant difference between the type of therapy given to lowering the IPSS-voiding. IPSS-Voiding a question in the IPSS group that assesses symptoms of lower urinary tract obstruction due to BPH. In the sample group monotherapy with prostate volume <30 mL, there was no inhibition of the enzyme 5-alpha reductase. This gives the process of forming dihydrotestosterone continue and prostate volume will be increased so that the symptoms of voiding the sample are slightly reduced, but the sample group receiver combination therapy with a prostate volume > 30 mL, occurred inhibition of the enzyme 5-alpha-reductase by a group of 5-Alpha Reductase Inhibitor. This gives the effect in suppressing the secretion dihydrotestosterone and prostate volume was expressed in a significant decrease in IPSS-voiding in the combination group. In accordance with the results of research, Wilt and N'Dow suggest

there is a significant association between combination therapy to decrease lower urinary tract symptoms due to BPH obstruction.⁸

Tables 5 and 6 explain the significant difference between the type of therapy given to lowering the IPSS-storage. Medical combination therapy patients with BPH LUTS provide a synergistic effect. Class of alpha-blockers inhibits the contraction of smooth muscles of the prostate excess while group 5-Alpha Reductase inhibitors work by inhibiting enlargement of the prostate volume. The second impact this may provide symptomatic relief in the form of a decrease in muscle contractions of the detrusor muscle overactivity that detrusor can be avoided. It is expressed as a decrease in IPSS scores greater-storage on a sample group of combination therapy according to the results of research.⁶

Tables 5 and 6 explain the significant difference between the type of therapy given to lowering the IPSS-storage. Medical combination therapy patients with BPH LUTS provide a synergistic effect. Class of alpha-blockers inhibits the contraction of smooth muscles of the prostate excess while group 5-Alpha Reductase inhibitors work by inhibiting enlargement of the prostate volume. The second impact this may provide symptomatic relief in the form of a decrease in muscle contractions of the detrusor muscle overactivity that detrusor can be avoided. It is expressed as a decrease in IPSS scores greater-storage on a sample group of combination therapy according to the results of research BPH LUTS.⁶

There are differences between the types of therapy given to lowering the IPSS-quality of life. Data from the study showed that the average score of the IPSS-QoL sample combination therapy group declined 2.56 points while the sample monotherapy group declined 1.68 points. Differences generated by the two groups was not too big for life quality assessment through only one question in the IPSS and cannot represent improvements in the quality of life of patients after the administration of drug therapy combination therapy works both improve the quality of life according to the results of research BPH LUTS.

There is a significant difference between the type of treatment given to the patient's prostate volume. The results of the study provide data on 23 samples (92%) the receiving monotherapy had a prostate volume <30 mL while the entire sample receiver has a combination therapy of prostate volume > 30 mL. Kyprianou (2003) explains, the

provision of medical monotherapy group alpha-blockers to reduce smooth muscle contraction as a dynamic component, can be used in patients with BPH LUTS with prostate volume <30 mL.⁹ Medical combination therapy with 5-ARI class as hormone inhibitor of 5-alpha-reductase, which has a major role in increasing the volume of the prostate, can be administered in patients with BPH LUTS with prostate volume > 30 mL accordance with Vincenzo research and Carmen.¹⁰

CONCLUSION

There is a difference in the effectiveness of the administration of Alpha-Blocker Selective monotherapy (SAB) in combination with 5-Alpha Reductase Inhibitor (5-ARI) to decrease the International Prostatic Symptoms Score (IPSS) in total, IPSS-Voiding reduction, reduction-Storage IPSS, IPSS-QoL reduction, and prostate volume in patients with BPH LUTS Bina Sehat Hospital in Jember, Paru Jember Hospital, and Bhayangkara Bondowoso Hospital.

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